The Management of Cancer of the Breast

JUSTIN J. STEIN, *M.D.*, Los Angeles

• **Radical mastectomy is excellent only for cases of operable breast cancer in which the tumor is limited to the breast or to the nodes in the axilla. That there is metastasis to the internal mammary lymph nodes in a high proportion of cases has been "overlooked" for many years. Also it is probable that metastasis occurs to the supraclavicular lymph nodes more often than is suspected. Hence the extended radical mastectomy operation leaves much to be desired. There has been no significant improvement in recent years in the mortality rate of mammary cancer.**

Simple mastectomy and thorough adequate postoperative radiation therapy have much to offer.

Treatment of "operable" breast cancer should be a cooperative effort of surgeon, radiation therapist and pathologist.

CANCER OF THE BREAST is the most common malignant neoplasm occurring in women in this country. There has been no significant change in the death rates from breast cancer in California from 1920 to 1954.[12]

One factor in reported improvements in five-year survival rates is that since patients are now selected for operation with greater care than previously, operation is less often done in inoperable cases. Although use of surgical procedures in inoperable circumstances probably increase the rate of growth of the cancer and shortens life, in some such cases simple mastectomy may be indicated to remove a large ulcerated lesion as a palliative measure.

Perhaps the most widely accepted and universally employed operation in cancer therapy is radical mastectomy in the expectation of removing the primary cancer, its immediate surrounding tumor bed and the adjacent lymphatic tissues.

For many hundreds of years cautery and the use of escharotic materials were the main means of treatment of breast cancer. During the nineteenth century various modifications of simple mastectomy procedures were introduced. None of these measures was adequate to control breast cancer.

In 1894 Halsted[3] described an operation which was destined to become, after some modifications, widely accepted. Halsted did not at that time advocate removal of the pectoralis minor muscle. He did recommend removal of the supraclavicular lymph nodes on the same side as the breast lesion, but this was not routinely done. Meyer,[11] in 1894, presented an improved operation for radical mastectomy in which he advocated the routine removal of the pectoralis minor muscle as well as the pectoralis major muscle. These two great surgeons, independently concentrating on the problem of the surgical cure of breast cancer, were both arriving at essentially the same conclusions. Halsted also began to routinely remove the pectoralis minor muscle. He also described how some of his assistants removed the supraclavicular lymph nodes and explored the anterior mediastinum.

From 1920 to 1945 the most notable change in breast cancer therapy was the more widespread use of radium and x-ray therapy as primary treatment, as an adjunct to surgical operation and for palliation in inoperable cases. During the same period the use of estrogenic and androgenic hormones was introduced as an additional means of palliation.

The period from 1945 to the present has been one of confusing statistics, with many contradictory articles appearing in the literature, and no significant decrease in breast cancer mortality.

During this period, there have been extensive discussions of the question of simple mastectomy plus radiation therapy (McWhirter),[10] whether extended radical surgical procedures should be done, and the use of hypophysectomy and bilateral oophorectomy and adrenalectomy for palliative breast cancer. Also the importance of defining the various stages of the disease and of attempting to eliminate unnecessary operation in inoperable cases has been stressed.

It is surprising that, although much has been known for many years about the lymphatic drainage of the breast and in particular about the internal mammary lymphatics, not until recent years has a good deal of studious attention been given to this very important chain of lymph nodes. The supraclavicular lymph nodes have been ignored to a lesser degree. Most surgeons have considered involvement of the supraclavicular lymph nodes to indicate inoperability—probably rightly so, for the internal mammary lymph nodes are also usually involved.

It is quite apparent that without biopsy of the supraclavicular lymph nodes and the internal mammary lymph nodes, the clinical criteria of opera-

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bility set forth by Steinthal and Portmann and as previously described by Haagensen, are entirely inadequate.

In a study of the regional breast lymphatic involvement Wyatt, Sugarbaker and Stanton[18] analyzed the results of extended radical operation in 60 cases of clinically operable breast cancer. They found that only the internal lymphatics were involved in seven cases and that both the axillary and internal mammary lymph nodes were involved in 12 additional cases. Routine radical mastectomy would have been ineffective in 19 of the 60 operated cases. They did not give data regarding the supraclavicular lymph nodes.

Urban[15] reported upon an analysis of 215 cases of radical mastectomy with en bloc resection of the internal mammary lymph node chain in continuity. There was one postoperative death. In 35 per cent of the cases the internal mammary lymph nodes were involved and in 50 per cent there was involvement of the axillary lymph nodes. In 7 per cent of the cases there was no extension beyond internal mammary lymph nodes. In 60 per cent of cases in which there was involvement of the axillary lymph nodes and the primary lesion was in the medial half of the breast, the internal mammary lymph nodes were involved; and there was internal mammary lymph node involvement in 40 per cent of cases in which the primary lesion was in the outer quadrant of the breast. In 42 per cent of Urban's cases, routine radical mastectomy would have been ineffective. Why biopsy of supraclavicular lymph nodes was not done was not stated, and it is possible that there may have been involvement of these nodes also in some cases. The incidence of supraclavicular lymph node involvement has been reported as high as 23 per cent.

MacGuffie[9] reported that, at Delafield Hospital, in 37.3 per cent of 371 cases of clinically operable breast cancer in which biopsy of internal mammary lymph nodes was done, involvement of the nodes was noted. At Presbyterian Hospital the proportion was 25.8 per cent of 450 such cases. In 110 cases biopsy of supraclavicular as well as internal mammary lymph nodes was carried out. In only two cases were the supraclavicular nodes involved without involvement of the internal mammary nodes. In 15 cases there was involvement of the internal mammary nodes but not the supraclavicular nodes.

Urban expressed belief that most of the lymphatic spread of breast cancer occurs by embolism rather than by permeation of the lymphatic vessels. He was also of the opinion that between 10 and 15 per cent of all primary breast cancers spread via the hematogenous route. Handley,[5] in 1922, believed that breast carcinoma spreads centrifugally in all directions from the point of origin by permeation of the lymphatic plexuses.

Any attempt to define the stages of breast cancer must depend upon pathological study. In the past, reports of methods of staging have made little mention of biopsy studies of the internal mammary lymph nodes. Realistic staging of operable breast cancer must be on a clinical, surgical and pathological basis. One must know the status of the lymph nodes in the supraclavicular, axillary and parasternal regions. There is increasing evidence that widespread metastasis may take place early in the course of the disease. Batson[1] described a system of vertebral veins which extend from the skull to the coccyx and it is possible that cancer cells may become widespread by passing through these veins without going through the lungs. Perhaps if bone marrow studies were done routinely on patients with mammary cancer the incidence of wide dissemination of metastatic cells would be found to be much higher than it is now thought to be.

Even if large firm nodes are palpable in the axilla, one must wait histological study before making a diagnosis. Haagensen and Stout[2] observed that in only 236 of 278 cases in which the axillary lymph nodes were thought to be involved, on the basis of clinical examination, was there microscopic evidence of metastasis. Hooper and McGraw[6] found microscopically demonstrable metastasis in only 111 of 145 cases in which there were palpable axillary lymph nodes. Conversely, in some 50 per cent of cases in which axillary nodes are not palpable before operation, metastatic cells are found upon examination of the excised nodes. It can be concluded that unless patients with breast cancer are operated upon and histological studies of the lymph nodes are carried out, no one can state with certainty whether or not the axillary lymph nodes are involved.

In a previous study, the author and co-workers,[13] utilized one of the accepted methods of defining the stages of breast cancer.* It was observed that approximately 50 per cent of the patients had inoperable cancer when first seen and in only about 20 per cent of cases was the lesion in Stage I. Eleven patients who had supraclavicular metastasis had radical mastectomy with dissection of the involved neck nodes, and none of them survived five years. It was thought to be a reasonable assumption that patients with supraclavicular metastasis probably have metastatic lesions elsewhere as well and are not suitable candidates for operation.

*Stage I, cancer confined to the breast; Stage II, cancer in the breast with metastasis to the axillary lymph nodes which are movable and with or without limited skin involvement of the breast; Stage III, fixation of the breast to the chest wall, metastasis to the supraclavicular lymph nodes, or distant metastasis.

Wangensteen and co-workers[16] reported the results of super-radical mastectomy done on 64 patients. The operation included excision of the supraclavicular, parasternal and mediastinal regional lymphatics. The operative mortality was 12.5 per cent. Thirty-seven or 57.8 per cent of the patients had metastatic cancer in the supraclavicular or mediastinal lymph nodes. Of 29 patients who were continuously observed, 17 were dead at the end of five years and only three of the remaining 12 were well.

Macdonald[8] expressed the belief that 55 per cent of patients with breast cancer have remote metastasis by the time the mammary lesions are detectable clinically, that in 20 per cent of cases the rate of growth is slow and the patients would live five years without treatment and that in the remaining 25 per cent of cases cure could be achieved by proper therapy, making a total of 45 per cent in which, theoretically, five-year survival would occur or could be brought about.

Urban[15] stated that the five-year salvage rate of patients with primary operable breast cancer treated by radical mastectomy is approximately 55 per cent in most of the large medical centers in this country. The five-year survival rate for 3,494 patients treated by radical mastectomy at the Memorial Hospital was 77.5 per cent in cases in which there was no axillary involvement and 39.4 per cent in cases in which axillary metastasis had occurred.

Handley and Thackray,[4] noting that "for the past 150 years isolated observers have been calling attention to the internal mammary lymph chain and its importance in the spread of carcinoma of the breast," but without offering convincing proof, began a study entailing biopsy of the internal mammary lymph node chain in association with routine radical mastectomy. Involvement of the internal mammary lymph nodes was noted in 41 of 139 patients (29 per cent) with "operable" carcinoma of the breast. In eight cases the internal mammary lymph nodes were involved without axillary invasion.

Whereas surgical treatment of breast cancer has been almost universally accepted, such has not been the case with radiation therapy.

During the past 20 years many improvements have been made in the techniques of therapy and particularly in the skill of the therapists. The work of McWhirter is an outstanding example of what can be done. Realizing that about 35 per cent of so-called "operable" breast cancers cannot be cured by the usual radical mastectomy because of internal mammary and supraclavicular lymph node involvement and that dissection of the axillary contents may actually spread the disease in some cases, McWhirter advocated simple mastectomy plus postoperative irradiation. He expressed belief that the metastatic lesions in the lymph nodes can be more readily destroyed by irradiation if the primary tumor is removed.

DISCUSSION

The extended or super-radical mastectomies will probably add little to the cure rate of breast cancer and there will be less need for them if radiation therapists and surgeons will work together to develop an effective regimen of therapy.

In the past it has not been uncommon for some surgeons to do inadequate operation and then refer the patient for radiation in the hope that any remaining cancer cells would be destroyed. While radiation therapy may in some cases and to some degree compensate for inadequate excision, it ought not be relied upon for this purpose.

The radiation therapist must be competent and willing to assume the responsibility for carrying out thorough adequate radiation therapy. It is difficult to sterilize breast cancer by radiation therapy, but it can be done. It may not always be necessary to sterilize all the cancer cells, for the effect of the radiation is not only directly upon the cancer cell but on the tumor bed also. The inherent resistance or immunity of the host against the cancer may be increased. Cases in point are two in which there was recurrence, in the surgical scar, long after radical mastectomy—21 years in one case, 32 in the other. It must be assumed that the cancer cells were lying dormant all those years until something happened to the host's natural resistance and the cancer cells began to grow again.

If radiation therapy is to be given probably the most controversial question is whether it is to be used preoperatively or postoperatively. I do not believe that sufficient evidence is available to justify the assumption that preoperative is superior to postoperative radiation therapy. Personal experiences with preoperative radiation have not justified its continued use. Giving radiation therapy before operation delays the removal of the primary lesions and on the other hand operation may be carried out too soon afterward to permit the maximum benefit from radiation.

Stein and co-workers[13] presented data to the effect that radical mastectomy and postoperative radiation materially increased the five-year survival rate. There are many reports in the literature by other investigators who have reached similar conclusions.

Surgical treatment is superior to irradiation for "operable" breast cancer when it is the only method of therapy to be used. Although the majority of surgeons in this country today may advocate radical mastectomy as the only method by which breast cancer can be successfully treated, newer concepts

in breast cancer therapy may change this attitude, particularly in light of the previously mentioned facts that the breast cancer mortality has not declined, that the internal mammary lymph nodes and the supraclavicular lymph nodes may also be involved in a large proportion of cases, that it is impossible to determine operability without biopsy of these nodes, and that the extended radical mastectomy operation also leaves much to be desired.

Surely, then, the radiation therapist has much to offer in dealing with patients who have mammary cancer if a planned program is worked out in cooperation with surgeons and pathologists. At St. Bartholomew's Hospital approximately one-half of the patients admitted with breast cancer are treated by radical mastectomy and about one-half by conservative operation and radiotherapy. The results of study of these cases will be reported after a sufficient number have been treated and observed long enough.[17]

Operations, such as hypophysectomy, bilateral oophorectomy and adrenalectomy, and the use of estrogenic and androgenic hormones are of considerable importance for palliation in far advanced breast cancer. However, criteria for determining the selection of patient and the optimum time for operations of the kind mentioned are not yet definitely established.

Castration, either by operation or by radiation, offers additional months of palliation to a relatively high proportion of patients with far advanced breast cancer.

Hormones now have been used long enough in the treatment of advanced cancer of the breast to permit conclusion that they are of considerable value. The estrogens are usually prescribed for postmenopausal and the androgens for pre-menopausal women. It is probably preferable to use each palliative measure to its fullest extent rather than combine two or more at one time. For example, castration may be beneficial for four to nine months, and then later hormonal therapy could be used.

University of California at Los Angeles School of Medicine, Los Angeles 24.

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Social Security Footnotes

THE LATE Robert A. Taft classified the Social Security Act as our greatest single step toward socialism.

—From the Department of Public Relations, American Medical Association